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CONTROL OF POSTOPERATIVE ADYNAMIC BOWEL IN DOGS BY ELECTRIC STIMULATION

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Control of adynamic ileus in the postoperative phase has long presented a challenge to medical investigators. Veno-clysis combined with gastrointestinal decompression, either by nasogastric intubation(1) or temporary gastrostomy(2, 3), has effectively withstood the test of time. The same, however, cannot be said for the various drug preparations intermittently in vogue.

It has been known for some years that adynamic bowel responds to electric stimulation. Katona et al.(4) in 1959 used a square wave current for direct stimulation of the intestine in animals and, later, in 15 patients. These workers introduced one positive electrode into the lumen of the duodenum and another into the rectum. A negative electrode was attached to the body at a distant site on the skin. They had the best results with stimuli of 30-40 volts at frequencies of 50-100 cycles/second applied over half-hour periods.

In the same year Sperling(5) treated three patients suffering from paralytic ileus by electric stimulation applied externally to the skin of the abdominal wall for half-hour periods with one-hour intervals. He reported successful return of intestinal activity in all cases, but did not accurately define the parameters of the stimulus.

Garry and Gillespie(6) and later Gillespie(7, 8) could elicit both mechanical and electrical responses from intestinal smooth muscle in vitro by applying a single stimulus to the extrinsic parasympathetic motor nerve of the rabbit colon. These workers also found that stimulation of the parasympathetic nerve at frequencies above two per second ablated the "driving" action of the parasympathetic nerve. Single stimuli, on the other hand, if applied to the extrinsic sympathetic inhibitor nerve of the rabbit colon had no effect, either mechanical or electrical, on spontaneous activity of the muscle. Repetitive sympathetic nerve stimulation at frequencies above ten per second, however, caused complete mechanical and electrical quiescence.

The primary aim of the present study was to determine whether direct electrostimulation of the bowel is a workable method of restoring peristalsis in dogs whose intestines have been rendered adynamic experimentally. Further aims, if results should prove encouraging, were (1) to arrive at the exact electric stimulus parameters giving optimal bowel responses; (2) to gauge the extent of bowel involvement with such a response; and (3) to determine the efficacy of these contractions in propelling intestinal contents aborally.

METHODS

Induction of intestinal paralysis. Initial studies were directed toward achieving in dogs a true intestinal atony over a period long enough for us to assume a uniform basic paralytic state. The bowel in 16 animals was rendered paralytic by one of several methods including isolation and/or denervation of intestinal loops, intestinal anoxia or localized hypothermia, intraluminal cocaine instillation, mesenteric neural paralysis, and induction of bile peritonitis--a method which, though radical, was found most consistently to induce paralytic ileus. At laparotomy, bile (15-20 ml.) was aspirated from the gall bladder and instilled into the peritoneal cavity. After 60-90 min. the bowels were exteriorized and one of two preparations was made.

Experimental preparations. The first type of preparation was effected in 30 animals for accurate determination of the electric stimulus parameters that would best reactivate local intestinal peristalsis. Separate long loops of jejunum and ileum were isolated; Teflon-coated, stainless-steel multistrand wire electrodes* were placed in the muscular layer of

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* Surgaloy # O Cardiac Suture, American Cyanimid Co., Danbury, Conn.

the bowel wall near the proximal ends of the loops, and intraluminal balloons were positioned a few centimeters distally (Figure 1).

The electrodes were linked to an electronic stimulator* capable of varying the frequency, pulse duration and voltage of the stimuli. The balloons were connected via a strain gauge+ to devices recording the bowel responses at a fast speed# and at a slow speedx. Calibration of the devices permitted recording of pressure changes from 0 to 40 mm. Hg. All mechanical activity thus picked up in the bowel represented local peristalsis, i.e., a propagated contractile response in the immediate vicinity of the electrodes.

The second type of preparation was set up in 15 dogs to establish whether such local peristalsis evoked by electrostimulation at the proximal level of the bowel could be propagated aborally, thus initiating similar activity at a distal level. Early steps in this preparation are the same: induction of bile peritonitis followed by bowel exteriorization after 60-90 min. Bowel continuity was maintained, however, and two balloons were placed: at the proximal level (in jejunum) and at the distal level (in ileum). Two wire electrodes were implanted in the bowel wall ten centimeters distal to the ligament of Treitz. Following jejunal electrostimulation, any peristaltic activity in the distal ileum could be recorded via its own balloon. Similarly, any local peristaltic activity in the jejunum could be picked up by the proximal balloon (Figure 2).

Electrical activity of intestinal musculature. Mechanical and electrical activity of various parts of the small intestine were simultaneously recorded during normal peristalsis as well as after electrostimulation in four animals. Mechanical activity was recorded via intraluminal balloons, and changes in electrical potential were detected via needle electrodes placed in the bowel wall, routed through a preamplifierz and recorded via a D. C. amplifier&. This apparatus permitted comparison of electrical activity at various small-intestine levels in the normal state and after electrostimulation.

X-Ray studies. Barium sulphate emulsion was instilled into the proximal jejunum by threading into it a gastrostomy catheter (Figure 2). Hourly X-Rays made it possible to follow the passage of the radiopaque medium through the bowel in both experimental animals and controls.

Histology. Following one day of repeated bowel stimulation dogs were sacrificed at intervals varying from one to 14 days. Specimens of intestinal tissue from the electrode site and distal levels were then examined microscopically.

RESULTS

In initial experiments an attempt was made to reactivate peristalsis by a single stimulus of moderate (50 msec.) to long (600-5000 msec.) duration. The degree of mechanical response, represented by a single contraction without propagation was directly proportional to the stimulus duration. This single contraction lasted only as long as the stimulus period.

Previous work done in this laboratory[9, 10] had conclusively shown the efficacy of repetitive, short-pulse-duration stimuli in activating musculature of the urinary bladder and diaphragm. Although not expecting a significant response to such stimuli from smooth muscle of the small intestine, we attempted to reactivate peristalsis by applying both short and long stimuli and comparing the results. The repetitive, short-pulse-duration stimuli were in this instance, too, definitely more effective (Figure 3). A train of monophasic pulse stimuli, which proved superior to biphasic, invariably initiated a peristaltic wave which was propagated disally 20-30 cm. beyond the electrode site, continuing 3-4 min. after cessation of the stimulus. Repeated experiments with isolated intestinal loops elucidated the following picture of the optimal stimulus. It was monophasic with a pulse duration of 5-7 msec.

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* Model S4D, Grass Instrument Co., Quincy, Mass.
+ Model P23Db, Statham Instrument Co., Los Angeles, Calif.
# Twin-Viso Recorder, Model 60-1300, Strain Gauge Amplifier, Model 64-500B, Sanborn Co., Cambridge, Mass.
x Recti-Riter, Texas Instruments, Inc., Houston, Texas.
z Type 122 Low-Level Preamplifier, Tektronix Inc., Portland, Ore.
& Model 64-300A, Sanborn Co., Cambridge, Mass.

(Figure 4). The pulse should be repeated at 40-70 cycles/second frequency (Figure 5). A 6-8 sec. stimulus-train duration invariably initiated peristaltic activity lasting 3-4 min. (Figure 6). At least 4-5 volts was needed to obtain an effective response (Figure 7). To keep electrical excitation at a minimum the lowest ranges producing effective contractions were used. These stimulus trains could be repeated 3-5 times at 3-4 min. intervals, and in each instance resulted in a satisfactory peristaltic response.

Changes in the electrical potential of intestinal smooth muscle were studied in situ and compared with mechanical changes. Electrical changes were recorded during normal spontaneous peristalsis, during the phase of adynamic ileus and after electrostimulation. Intraluminal pressure readings and electrical changes in the jejunum during normal peristalsis revealed an activity cycle of about four minutes, whereas the pattern in the ileum was more irregular. After electrostimulation the potential changes were found to closely resemble those obtained during normal peristalsis. As with mechanical changes, these continued 3-4 min. after cessation of the stimulus.

Once the optimal stimulus parameters had been accurately determined, the next step was to learn whether electrostimulation at a proximal level would induce propagation of peristaltic activity throughout the entire small intestine. To this end the bowel was experimentally prepared by the second method described earlier. Results with electrodes placed at different intestinal levels pointed to the upper jejunum, 10-15 cm. distal to the ligament of Treitz, as the best implantation site. This finding is in accord with Keith's hypothesis[11] of three pacemakers in the small intestine, of which one is at the level of the ligament of Treitz. Also, it was found that positioning of the electrodes 1-2 cm. apart gave the best results.

In eight dogs undergoing electrostimulation of the proximal jejunum (i. e., repetition of the stimulus train 3-4 times at 3-4 min. intervals), the peristaltic waves evoked locally spread along the bowel for 20-30 cm. but then disappeared, leaving the distal intestine still paralyzed. On the chance the bowel distention by an inert substance might facilitate the forward propulsion of a mucosa-stimulating factor, 50-100 cc. of air was introduced into the bowel via a gastrostomy catheter. Results following stimulation were negative.

At this stage it was felt that bile peritonitis caused too severe a degree of atony to permit diffuse peristaltic reactivation. A less severe degree of intestinal paralysis was achieved in the next seven dogs by merely exposing the bowel for two hours. This condition more closely resembled postoperative ileus in human patients. Intestinal loops were prepared and balloons placed, but electrostimulation was not started until intraluminal pressure readings had established the existence of complete mechanical quiescence of both ileum and jejunum for at least one hour. In four of the seven animals peristaltic activity was reactivated in the distal ileum following electrostimulation of the proximal jejunum (Figure 8). This finding seems to suggest that widespread reactivation may depend to some extent on residual muscular tonus of the intestine. Should the method be employed clinically, it appears that electrostimulation must be started early in the postoperative period and that it should be envisioned as a prevention rather than a cure for paralytic ileus.

Serial barium studies done in experimental and control animals revealed an earlier evacuation of small bowel contents in the former group.

Microscopic examination of the bowel in animals sacrificed at varying intervals following electrostimulation revealed no alteration of the normal anatomy in distal intestinal segments. At the electrode implantation sites a mild to moderately severe degree of inflammatory reaction was noted depending on the time lapse following stimulation.

We believe that with further refinement this method will have future clinical application.

REFERENCES

1. Wangensteen, O. H. Intestinal Obstructions. 3rd Ed., Springfield, Ill., Charles C. Thomas, p. 758, 1955.
2. Farris, F. M. and Smith, G. K. An evaluation of temporary gastrostomy--a substitute for nasogastric suction. Ann. Surg., 144:475, 1956.
3. Hurwitz, A. A new dual-purpose gastrostomy tube. Arch. Surg., 77:79, 1958.
4. Katona, F., Benyó, I. and Láng, I. Experiences in the application of quadrangular current for direct electrical treatment of adynamic ileus and acute postoperative intestinal paralysis. Wien. Klin. Wchschr., 71:918, 1959.
5. Sperling, R. Paralytic ileus and treatment with electrical current. Muench. Med. Wchschr., 101:822, 1959.

6. Garry, R. C. and Gillespie, J. S. The responses of the musculature of the colon of the rabbit to stimulation, in vitro, of the parasympathetic and of the sympathetic outflows. J. Physiol., 128:557, 1955.
7. Gillespie, J. S. Spontaneous mechanical and electrical activity of intestinal smooth muscle cells and their response to stimulation of the extrinsic parasympathetic nerves. J. Physiol., 155:59P, 1961.
8. Gillespie, J. S. Spontaneous mechanical and electrical activity of stretched and unstretched intestinal smooth muscle cells and their response to sympathetic-nerve stimulation. J. Physiol., 162:54, 1962.
9. Kantrowitz, A. and Schamaun, M. Paraplegic dogs: Urinary bladder evacuation with direct electric stimulation. Science, 139:115, 1963.
10. Cohen, R. and Kantrowitz, A. Personal communication.
11. Keith, A. A new theory of the causation of enterostasis. Lancet, 2:371, 1915.

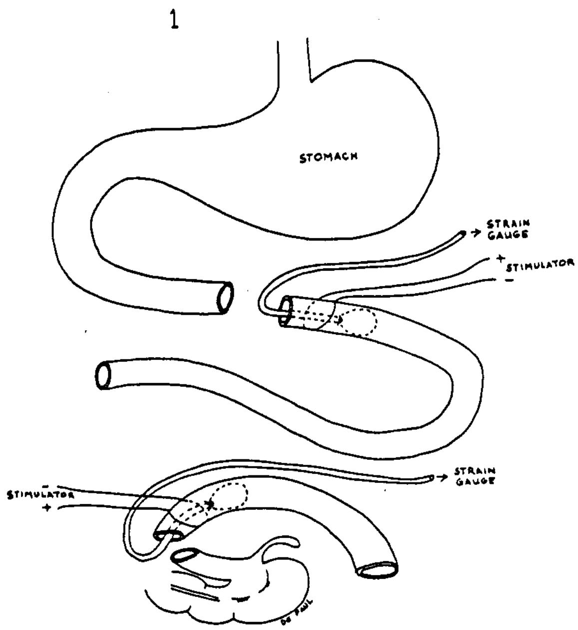

Figure 1. Experimental preparation with isolated intestinal loops.

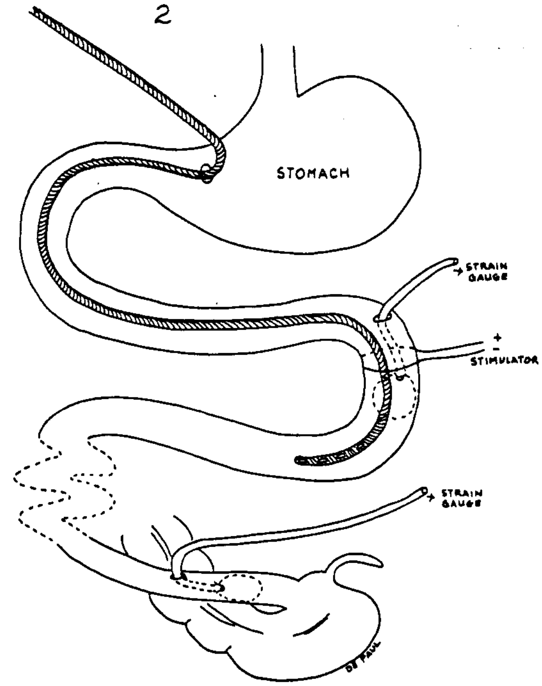

Figure 2. Experimental preparation with preservation of intestinal continuity.

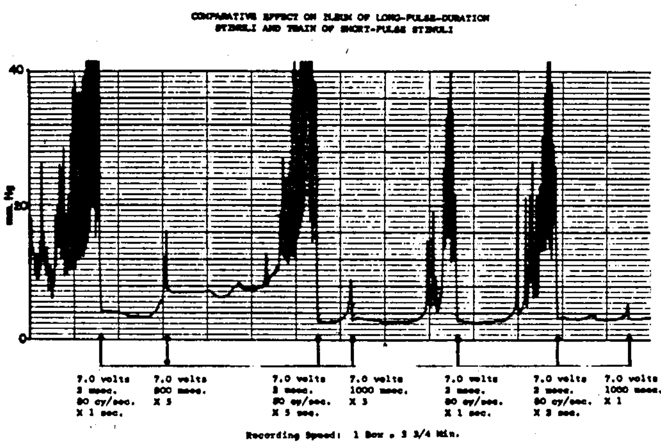

Figure 3. Comparative effect of long-pulse-duration stimuli and train of short-pulse stimuli.
(All graphs read from right to left.)

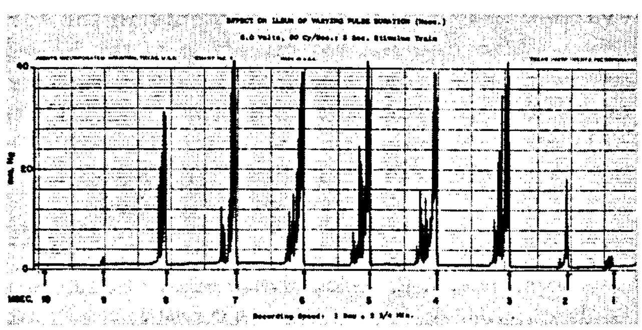

Figure 4. Effect on ileum of pulse duration varying between one and 10 msec. (6.0 volts, 80 cycles/sec., and 2 sec. stimulus train.)

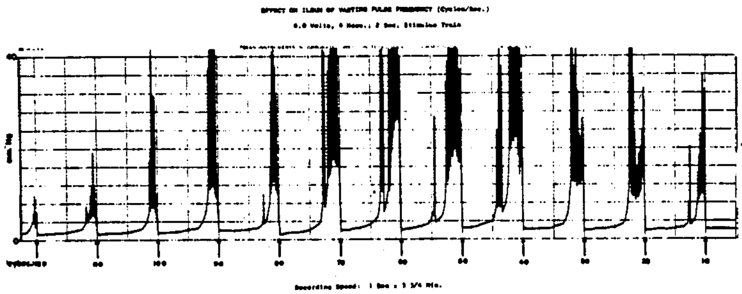

Figure 5. Effect on ileum of pulse frequency varying between 10 and 120 cycles/sec. (6.0 volts, 6 msec., and 2 sec. stimulus train).

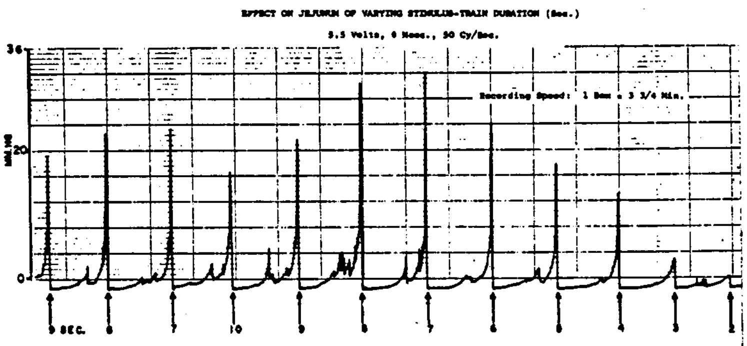

Figure 6. Effect on jejunum of stimulus-train duration varying between 2 and 9 sec. (5.5 volts, 6 msec., and 50 cycles/sec).

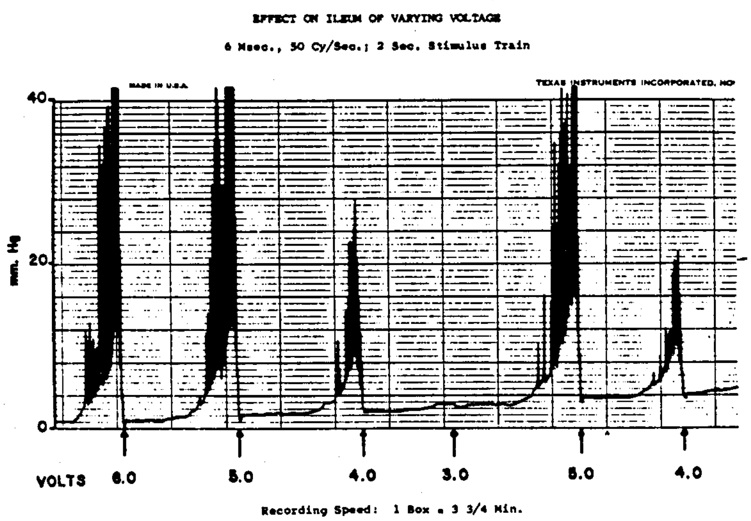

Figure 7. Effect on ileum of voltage varying between 3.0 and 6.0. (6 msec., 50 cycles/sec., and 2 sec. stimulus train).

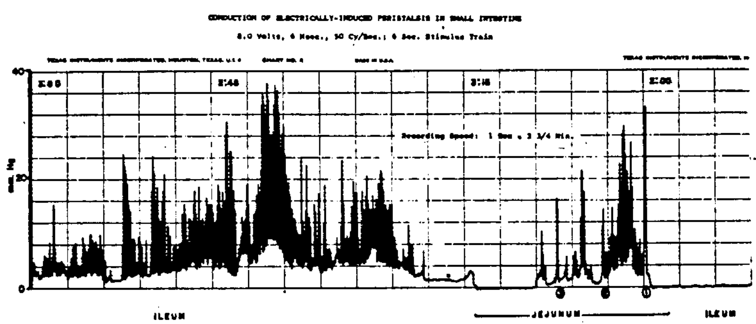

Figure 8. Propagation of electrically induced peristalsis in small bowel. (8.0 volts, 6 msec., 50 cycles/sec. and 6 sec. stimulus train).

DR. KOLFF: I wonder how many people will now say: "gee, I always wanted to do that. It seems so obvious, and it's so surprising that I've never heard of it before." We wish you luck.

DR. OMURA: Excitation only happened in our experiments between two electrodes, so the position in the intestine may be very important. Also, we have compared different wave forms such as regular sine waves, triangular waves, saw tooth waves, and also spikes. We could not find much difference in effect between the shapes used, but frequency was very important. If we used a high frequency, this produced peristalsis on the intestine that the electrodes touched.

DR. BONNABEAU: I was very happy to see this worked out experimentally this way. We did much the same thing several months ago. We were interested more in the clinical application so we didn't do a thorough experimental study of the complete bowel, we actually looked more to the stomach, and we were able to find very much the same thing you did; the same type of stimulating frequency, etc. We then used a small catheter actually just a straight nasal gastric tube with a thin wire running inside it and a small uni-polar electrode at one end. Another flat plate placed on the abdomen is used as an indifferent electrode and is then hooked up to the small stimulating unit, which I have here in my hand.

We found that by stimulating the antrum of the stomach, we could induce peristalsis postoperatively, and we've used this in about 40 patients up until now, and it has worked very well. We've been able to have patients post-operatively pass the first stool in approximately 16 hr. after being operated on. These were Billroth II gastrectomies, bowel resections, etc.

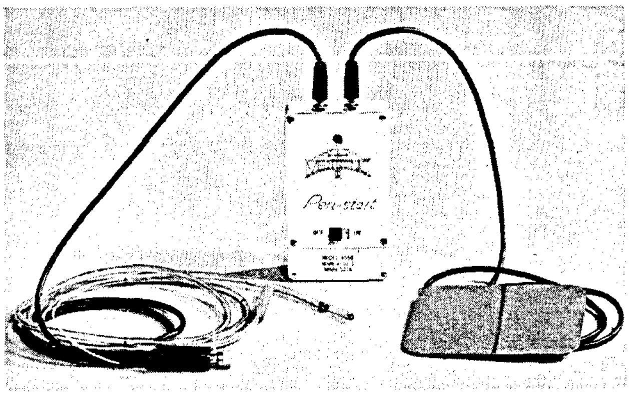

Figure 1.

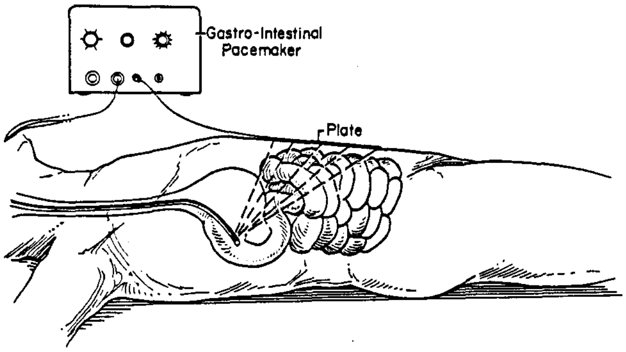

Figure 2.

We've also found out that by stimulation of the colon we're able to do approximately the same thing. Colon stimulation seems to stimulate the rest of the bowel.

Figure 2 is the basic diagram of the unit in place in a patient.

DR. KOLFF: Is it available?

DR. BONNABEAU: It's available for clinical use.

DR. KOLFF: I tried to ask if it was painful to the patient, does it hurt when you stimulate?

DR. BONNABEAU: Excuse me, I didn't hear you. Actually, when we first started using this, we used in on ourselves, and a stimulus of 20 milliamps or so was painful; we use it at present at about 10 milliamps, and patients don't feel anything.

DR. KANTROWITZ: I think since the group from Minnesota has brought up their clinical experience, I might as well report what clinical experience we have had with Dr. deVillier's procedure.

We have used this now in four patients. In all four it appeared to be very effective, judging by physical signs, such as the appearance of borborygmi and the passage of flatus much earlier than one would normally expect. We have used it in three patients now where we have resected aortic aneurysms, and in one patient where colon surgery was performed, and if one goes above six or seven volts, the patients do complain of some sensation, but below this level, which appears to be effective, there isn't any sensation at all.

DR. SCHREINER: What was the earliest time post-op?

DR. KANTROWITZ: One-half hour.

DR. KOLFF: I feel that this is an extremely important contribution.

May I ask do we have the honor of having it first reported here or has it been reported somewhere else too.

DR. deVILLIERS: It was reported to the American Surgical Association about a week and a half or so ago.

DR. KOLFF: I forget about that one.

DR. KANTROWITZ: This same paper was reported to the New York Surgical Society about a month and a half ago.

DR. KOLFF: Congratulations just the same.

I think it may be very useful in peritoneal lavage. Very often patients with peritoneal lavage have some degree of atony of the intestinal tract, it's one of the worries, and the artificial kidney people that didn't stay on are now being punished for not being here.